



General

Guideline Title

Pain: assessment, non-opioid treatment approaches and opioid management.

Bibliographic Source(s)

Hooten M, Thorson D, Bianco J, Bonte B, Clavel Jr A, Hora J, Johnson C, Kirksson E, Noonan MP, Reznikoff C, Schweim K, Wainio J, Walker N. Pain: assessment, non-opioid treatment approaches and opioid management. Bloomington (MN): Institute for Clinical Systems Improvement (ICSI); 2016 Sep. 160 p. [473 references]

Guideline Status

This is the current release of the guideline.

This guideline updates previous versions: Thorson D, Biewen P, Bonte B, Epstein H, Haake B, Hansen C, Hooten M, Hora J, Johnson C, Keeling F, Kokayeff A, Krebs E, Myers C, Nelson B, Noonan MP, Reznikoff C, Thiel M, Trujillo A, Van Pelt S, Wainio J. Acute pain assessment and opioid prescribing protocol. Health care protocol. Bloomington (MN): Institute for Clinical Systems Improvement (ICSI); 2014 Jan. 44 p. [76 references]

Hooten WM, Timming R, Belgrade M, Gaul J, Goertz M, Haake B, Myers C, Noonan MP, Owens J, Saeger L, Schweim K, Shteyman G, Walker N. Assessment and management of chronic pain. Bloomington (MN): Institute for Clinical Systems Improvement (ICSI); 2013 Nov. 105 p. [168 references]

This guideline meets NGC's 2013 (revised) inclusion criteria.

Regulatory Alert

FDA Warning/Regulatory Alert

Note from the National Guideline Clearinghouse: This guideline references a drug(s) for which important revised regulatory and/or warning information has been released.

- [August 31, 2016 – Opioid pain and cough medicines combined with benzodiazepines](#) : A U.S. Food and Drug Administration (FDA) review has found that the growing combined use of opioid medicines with benzodiazepines or other drugs that depress the central nervous system (CNS) has resulted in serious side effects, including slowed or difficult breathing and deaths. FDA is adding Boxed Warnings to the drug labeling of prescription opioid pain and prescription opioid cough medicines and benzodiazepines.

Recommendations

Major Recommendations

Note from the National Guideline Clearinghouse (NGC) and the Institute for Clinical Systems Improvement (ICSI): The recommendations for pain assessment, non-opioid treatment approaches and opioid management are presented in the form of a table with a list of evidence-based recommendations and 4 algorithms, accompanied by detailed annotations. The algorithm is provided in the original guideline document at the ICSI Web site for Pain: Assessment, Non-Opioid Treatment Approaches and Opioid Management (see the "Guideline Availability" field).

Assess Quality-of-Life, Function and Pain

Work Group Recommendation: Use validated tools to assess and document the patient's functional status, quality-of-life and pain intensity.

- Benefit: Standardized assessment tools offer consistency for the documentation of pain intensity and physical function.
- Harm: Clinicians may rely too much on tools, which are only one component of the clinical evaluation.
- Benefit-Harms Assessment: Validated tools provide accurate information for the creation and the ultimate success of progress with a treatment plan. If no tools are utilized, the assessment of the patient becomes subjective.
- Relevant Resources: Keller et al., 2004

Determine the Pain Generator

Opioid-Related Alterations in Pain Processing and Acute Opioid Withdrawal

Work Group Recommendation: Patients presenting with an indeterminate pain generator should be assessed for exposure to opioids in the past and current opioid use. Providers should consider checking the prescription monitoring program for patients presenting with pain if his or her past opioid exposure is uncertain.

- Benefit: Patients with past exposure to opioids have a different set of expectation and risks, and may suffer from a different set of pain generators than those who are opioid naïve. Patients with past exposure to opioids may have known drug interactions or adverse effects that would affect management decisions.
- Harm: It will take additional time to discuss opioid status during the patient encounter.
- Benefit-Harms Assessment: As the proportion of Americans being exposed to opioids grows, the assessment of opioid exposure becomes increasingly important in patients presenting with pain. Knowing if the patient has been exposed to opioids at the time of his or her pain presentation provides both diagnostic and management information. The prevalence of opioid use is great enough to now justify the burden of assessing opioid use routinely in patients who present with an indeterminate pain generator.
- Relevant Resources: Nuckols et al., 2014; Cicero et al., 2014; Chu, Clark, & Angst, 2006

Dental/Orofacial Pain Diagnosis and Treatment

Treatment

Work Group Recommendation: Prescribe ibuprofen and acetaminophen combination as first-line treatment for dental pain. The referring medical clinician for acute dental pain should not routinely prescribe opioid medications.

- Benefit: Public and patient safety. The combination of ibuprofen and acetaminophen is more effective and has fewer side effects than opioids.
- Harm: None known because it gives the clinician an effective non-opioid option for pain relief.
- Benefit-Harms Assessment: Compassionate, non-opioid oral/facial pain relief before and after the treatment of the underlying cause of the pain can almost always be accomplished and avoids the serious risk that accompanies every dose of an opioid medication prescribed.
- Relevant Resources: Moore & Hersh, 2013

Assess Physical and Behavioral Health Comorbidities

Behavioral Health Assessment

Work Group Recommendation: Assess for behavioral health comorbidities in patients with chronic pain.

- Benefit: Could reveal key barriers in patient's underlying suffering and improve treatment outcome.
- Harm: Could re-expose patient to sense of being traumatized and thereby contribute to flashbacks, nightmares, emotional numbing or outburst.
- Benefit-Harms Assessment: Correct identification of potential underlying behavioral conditions allows for more efficient treatment and the

resolution of important contributing factors that could otherwise complicate chronic pain conditions.

- Relevant Resources: Hooten, 2016; Janssens et al., 2015; Asmundson & Katz, 2009

Substance Abuse, Dependence, and Addiction

Work Group Recommendation: Consider screening patients for substance use disorders when there is an unclear etiology of pain.

- Benefit: Many sources of pain are caused directly or indirectly by the use of addictive substances. Pain treatment decisions are greatly affected by the presence of a substance use disorder (SUD). Screening, brief intervention and referral to treatment (SBIRT) is a routine recommendation for doctors in primary care and emergency care settings, and a pain presentation should trigger an SBIRT.
- Harm: Patients may feel that they are treated with suspicion. Performing a substance use disorder screening for patients in pain will consume provider time.
- Benefit-Harms Assessment: Substance use disorder informs the diagnosis and complicates the treatment of pain in many patients and many settings. There will be numerous patients screening negative for whom the screening was not necessary. But for those who screen positive, the benefit is more appropriate care.
- Relevant Resources: Han et al., 2015; Hooten et al., 2015; Jones, 2013; Juurlink & Dhalla, 2012; Sehgal, Manchikanti, & Smith, 2012; Bohnert et al., 2011; Liebschutz et al., 2010; Chou et al., "Opioids," 2009; Martell et al., 2007

Develop Pain Treatment Plan

Work Group Recommendation: When feasible, a multidisciplinary approach is recommended for treating the patient with pain, especially chronic pain.

- Benefit: The complexities of chronic pain require a complex biopsychosocial approach using a multidisciplinary care team.
- Harm: Not all clinicians have access to psychologists, addiction treatment, physical therapy, or interventional specialists.
- Benefit-Harms Assessment: The chronic pain patient will benefit from multidisciplinary care, even if it is done in a virtual setting and managed by the primary clinician.
- Relevant Resources: International Association for the Study of Pain, 2014; Gatchel & Okifuji, 2006

Psychotherapy Strategies

Work Group Recommendation: Psychotherapy, such as cognitive behavioral therapy or mindfulness-based stress reduction, is recommended for patients with a chronic pain diagnosis.

- Benefit: Builds patient adherence to a treatment plan. Helps patients replace maladaptive cognitions and behaviors with more adaptive ones.
- Harm: Minimal (if any) adverse side effects of psychotherapy.
- Benefit-Harms Assessment: This could help bring a more complete sense of healing for the patient. Studies show decreased pain, more active and better quality of life, and better general health. Lack of clinicians with expertise or training could pose an access problem.
- Relevant Resources: International Association for the Study of Pain, 2014; Kamper et al., 2014; Castro et al., 2012; Grossman et al., 2007; Gillis et al., 2006; Turner, Mancl, & Aaron, 2006; Broderick, Junghaenel, & Schwartz, 2005; Smyth & Helm, 2003

Physical Rehabilitation Modalities

Work Group Recommendation: Exercise should be a component of the treatment for a patient with chronic pain.

- Benefit: Exercise improves chronic pain symptoms and functional status, and bolsters overall health and sense of well-being.
- Harm: There may be potential exacerbation of underlying, or undiagnosed, musculoskeletal injury, cardiovascular or neurologic disease.
- Benefit-Harms Assessment: There is not one particular exercise that is superior, and the optimal frequency has not been demonstrated. The current evidence suggests at least 2 to 3 exercise sessions per week are necessary for clinical benefit.
- Relevant Resources: Falla et al., 2013; Cuesta-Vargas et al., 2011; Standaert et al., 2011; Dufour et al., 2010; Hall et al., 2008; Hurwitz et al., 2008; Hayden et al., 2005

Work Group Recommendation: Passive modalities should be performed only as an adjunct to a concomitant active physical therapy or exercise program.

- Benefit: Passive physical treatments provide short-term pain relief and potential medium-term benefit.
- Harm: There is minimal risk of harm when applied by trained practitioners.
- Benefit-Harms Assessment: Recommend passive treatments only as a complement to an active therapy or exercise program.
- Relevant Resources: Vincent et al., 2013; Standaert et al., 2011

Work Group Recommendation: Extending physical therapy beyond 8 to 12 weeks for chronic pain patients should be based on objective clinical improvement.

- Benefit: Physical therapy facilitates rehabilitation and optimizes functional performance in chronic pain patients when used appropriately.
- Harm: There may be additional resources and cost for patients and service providers without evidence of improved outcomes.
- Benefit-Harms Assessment: An active physical therapy program is recommended. Deconditioned pain patients should begin with a graded or progressive physical therapy program to minimize risk of exercise associated injury, and improve patient engagement and compliance.
- Relevant Resources: Cuesta-Vargas et al., 2015; Cramer et al., 2013; Falla, 2013; Standaert et al., 2011; Dunder et al., 2009; Koumantakis, Watson, & Oldham, 2005; Rainville et al., 2002

Pharmacologic Treatment

Non-Opioid Medications

Work Group Recommendation: Sedative hypnotics including benzodiazepines and carisoprodol should be rarely used and if so for short-term (<1 week) treatment of muscle spasms related to acute pain. Use of non-sedative hypnotic muscle relaxants are of low benefit, but if used, limit to less than four weeks. Do not use carisoprodol for pain.

- Benefit: Skeletal muscle relaxants are better than placebo but not more effective than nonsteroidal anti-inflammatory drugs (NSAIDs) in the treatment of low back pain. Sedative hypnotics are effective for treating anxiety and muscle spasms in acute pain.
- Harm: Muscle relaxants are central nervous system (CNS) depressants and cause additive sedation and other adverse effects, especially in combination with opioids. Sedative hypnotics have significant side effects, specifically in the geriatric population. Additive side effects when taken with other CNS depressants are potential for dependence and withdrawal symptoms.
- Benefit-Harms Assessment: Muscle relaxants should not be used as the standard first-line treatment but may provide short-term benefit in some patients. Risk of significant side effects and potential for dependence and withdrawal outweigh the benefit for long-term use.
- Relevant Resources: American Geriatrics Society 2015 Beers Criteria Update Expert Panel, 2015; Gray et al., 2015; Petrov et al., 2014; Richards et al., 2012; Liu et al., 2010; Chou et al., 2007; van Tulder et al., 2003

Opioid Management

Risk Assessment

Before initiating opioids for pain, providers should seek a specific diagnostic cause of the pain, and document objective findings on physical exam or other objective tests.

Risk Assessment Tools

Work Group Recommendation: Opioid risk assessment tools and knowledge of opioid-related risks should be used in combination with the overall clinical picture to guide care, including the decision to prescribe as well as how closely to monitor.

- Benefit: Assessment of opioid-related risks may help physicians weigh risks against benefits when deciding if to prescribe opioids. In addition, knowledge of the risk factors for the various adverse outcomes of opioids helps physicians determine the intensity of monitoring and follow-up for patients. Reviewing the risks also serves as a patient education tool.
- Harm: The use of risk assessment tools does not have an adequate sensitivity or specificity to predict opioid-related harms or to rule them out. Universal precautions should be used for all patients receiving opioids. Using risk assessment tools has not been shown to improve clinical outcomes. Risk assessment tools should not be used to exclude patients with mental health or addictive disorders from proper treatment of pain.
- Benefit-Harms Assessment: Used correctly, knowledge of the risks of opioid related harm, including risk assessment tools, can help providers more carefully monitor those at high risk. In cases where the risk/benefit of opioids is uncertain, risk assessment can tip the provider against use of opioids. These tools can also be used incorrectly; for instance, they cannot be used to assure a patient that he or she has no risk, and they should not be used to exclude mentally ill patients from routine treatment of pain.
- Relevant Resources: Volkow & McLellan, 2016; Wasan et al., 2015; Argoff, Kahan, & Sellers, 2014; Jones et al., 2014; Atluri, Akbik, & Sudarshan, 2012; Jones et al., 2012; Moore et al., 2009

Special Populations

Pregnant, Lactating or Women of Childbearing Age

Work Group Recommendation: Prior to prescribing opioids, women of childbearing age should be counseled on the risks of opioids in pregnancy

and on contraception, and offered pregnancy testing.

- Benefit: There may be teratogenic effects to opioids. Neonatal abstinence syndrome is costly and burdensome on the family and medical system. Opioid withdrawal in pregnancy may compromise obstetrical outcomes. Many opioid prescribers are uncomfortable continuing opioids in pregnancy.
- Harm: There is no harm in counseling the patient. Counseling takes additional time during the patient encounter.
- Benefit-Harms Assessment: The use of opioids in women of childbearing age, and in pregnancy, is widespread. Most pregnancies are unaffected by exposure to low dose or intermittent opioids. Some pregnancies are affected, including a low rate of teratogenicity, rising neonatal abstinence syndrome rates, and challenging the comfort of the opioid prescriber and the obstetrician. A discussion on the risks and benefits of opioids use seems prudent for this population.
- Relevant Resources: Desai et al., 2015; Han et al., 2015; Desai et al., 2014; Maeda et al., 2014; Whiteman et al., 2014; Yazdy et al., 2013; Broussard et al., 2011

Geriatrics

Work Group Recommendation: Geriatric patients should be assessed for risk of falls, cognitive decline, respiratory malfunction, and renal malfunction before receiving opioids. If impairment or risk is detected in a geriatric patient, initiation of opioids should be at half the usual dose.

- Benefit: Doing a unique assessment for geriatric patients is important because of this group's unique vulnerabilities. Lowering the dose of opioids may lower the risk of opioid-related harm, such as falls and respiratory suppression, in this population.
- Harm: Geriatric patients are a diverse group of patients, some more fragile and others more robust. They should not be treated as having equal risk of opioids as a group. The most fragile geriatric patients may also have contraindications to the common alternatives to opioids. This may lead to undertreatment of pain.
- Benefit-Harms Assessment: Like many of the high-risk populations, using special precautions and lower doses in the geriatric population lowers the risk of opioid-related harms while also risking undertreating pain.
- Relevant Resources: Han et al., 2015; Makris et al., 2014; Rubin, 2014; Rolita et al., 2013; Saunders et al., 2010; Solomon et al., 2010; Spector et al., 2007; Vestergaard, Rejnmark, & Mosekilde, 2006

Prescriber Responsibility with Opioid Prescription

Patient Education and Shared Decision-Making

Work Group Recommendation: The first opioid prescription should include patient education, shared decision-making and assessment for related risks.

- Benefit: Appropriate informed consent and shared decision-making should occur early in the course of prescribing opioids. Much opioid-related harm, including overdose, can happen early in the course of pain treatment. Aberrant behaviors and comorbidities should be identified as early as possible. Patient expectations should be set early in the course of opioid treatment.
- Harm: Patients may feel that they are being treated with suspicion. Very low-risk patients will be asked to spend time and energy to receive opioids. Clinician time and clinical resources will be dedicated early in the course of opioid prescribing.
- Benefit-Harms Assessment: Early patient education, re-education, screening for comorbidities and detecting aberrant behaviors represent a burden to patients and clinicians that is outweighed by the benefit of promptly addressing opioid-related harms and providing the patient with up-to-date and thorough education about the risks of opioids. This approach emphasizes universal precautions.
- Relevant Resources: Hooten, Lamer, & Twyner, 2015

Safe Use, Storage and Disposal

Work Group Recommendation: Patients newly on opioids, or having recently had their opioid dose increased, should be advised not to operate heavy machinery, including driving a car, or participate in other work or home activity that may be affected by the sedating effect of opioids. An individualized approach that weighs the risks and benefits of driving and other activities should be taken with patients chronically on stable opioids who have tolerance and do not show evidence of sedation.

- Benefit: The sedating effect of opioids impairs one's ability to drive a motor vehicle and carry out other tasks similarly sensitive to wakefulness and reaction time. As a safety measure, it is important to clearly warn patients about the risk to themselves and others performing potentially dangerous tasks while on opioids. With the development of opioid tolerance and the absence of sedation, studies have shown that patients can safely drive a motor vehicle.
- Harm: Driving, work and household prohibitions can be burdensome and may prevent timely return to normal life activities.
- Benefit-Harms Assessment: The risk to public safety of patients newly on opioids operating motor vehicles and carrying out similar tasks

clearly outweighs the inconvenience to the individual on opioids. Determining when the patient has enough tolerance to safely drive is a subjective judgment call, and prescribers should err on the side of caution and document carefully.

- Relevant Resources: National Highway Traffic Safety Administration, 2016; Schisler, Groninger, & Rosielle, 2012

Work Group Recommendation: Clinicians should discuss storage and opioid disposal options with patients at the first opioid prescription and in follow-up visits as needed.

- Benefit: Proper storage and disposal can reduce opioids involved in diversion and overdose.
- Harm: There are no easy options for disposal of opioids.
- Benefit-Harms Assessment: Considering the great harm of excess opioids to the community, every opioid prescription should be accompanied with storage and disposal information. Disposal information is everchanging and complicated. While communicating the information is not highly burdensome, staying abreast of the latest information may be.
- Relevant Resources: Dowell, Haegerich, & Chou, 2016; Centers for Disease Control and Prevention, 2010

Opioid Formulation

Work Group Recommendation: Long-acting opioids should be reserved for patients with established opioid tolerance and in whom the prescriber is confident of medication adherence. Long-acting tamper-proof formulation for opioids is preferred.

- Benefit: Tamper proof formulations of opioids have been linked to decreased diversion, abuse and death, when used for chronic pain. See the [U.S Food and Drug Administration \(FDA\) site](#) for more information. When used for acute pain, or in patients without opioid tolerance, long-acting opioids are associated with inadvertent opioid overdose death. Methadone pharmacology is complicated, and its routine use is associated with overdose death.
- Harm: Tamper-proof formulations may not be covered or may have greater copay. For some situations, such as sleep, the duration of short-acting opioids is insufficient to treat pain.
- Benefit-Harms Assessment: While there may be some select circumstances where use of long-acting opioids seems appealing in acute pain, they have failed to show benefit and are associated with overdose death. Using methadone in acute or chronic pain is associated with harm, owing to its unique pharmacology. If long-acting opioids are indicated, using a tamper-proof formulation may improve outcomes.
- Relevant Resources: Hwang, Chang, & Alexander, 2015; Argoff, Kahan, & Sellers, 2014; Cassidy et al., 2014 ; Havens et al., 2014; Sessler et al., 2014; Butler et al., 2013; Coplan et al., 2013; Severtson et al., 2013; Manchikanti et al., 2012; Severtson et al., 2012; Dhalla et al., 2009

Patient-Provider Agreement (PPA)

Work Group Recommendation: Initiate a PPA at the time an opioid is prescribed for:

- High-risk patients
- Daily use of opioids >30 days
- Patient transfers to a new clinic already on opioids
- Episodic use up to 90 days over the course of a year
- If none of the above, initiate a PPA after 90 days of opioids is prescribed

Benefit: PPAs provide the patient with a clear set of expectations in writing.

Harm: It has not been demonstrated that PPAs improve clinical outcomes. PPAs may be used as a pretext for dismissing undesirable patients.

Benefit-Harms Assessment: PPAs have not been proven an effective medical intervention; however, they provide a clear set of expectations for patients and clinicians. Executed and used correctly, a PPA can help prevent patient provider disagreement and allow the clinic to insist on consistent and universal practices for opioid-receiving patients. When done incorrectly, a PPA may cause patients to be dismissed from care without appropriate referrals or follow-up.

Relevant Resources: Dowell, Haegerich, & Chou, 2016; Hooten, Lamer, & Twyner, 2015; Noble et al., 2010; Starrels et al., 2010; Arnold, Han, & Seltzer, 2006

Consider Offering Naloxone

Work Group Recommendation: Clinicians should consider offering the patient and close contacts (family/friends/caretaker) a naloxone kit.

- Benefit: Community access to naloxone may save lives that would otherwise be lost to opioid overdose death. Many states explicitly support and legally protect this use of naloxone in law.

- **Harm:** Naloxone is not a treatment of the underlying causes of opioid overdose. Some forms of overdose are not reversed by a single dose of naloxone. Inducing opioid withdrawal may cause discomfort or other adverse effects. Training is required. Emergency services should be called when naloxone is used. Widespread use of naloxone may compromise its supply for those who need it the most.
- **Benefit-Harms Assessment:** Home use of naloxone can save the life of a person who would otherwise die from an opioid overdose, but it does not correct the underlying cause of the overdose, and it requires training to use appropriately.
- **Relevant Resources:** Coffin et al., 2016; Coffin & Sullivan, 2013; Centers for Disease Control and Prevention, 2012; Albert et al., 2011; Yokell et al., 2011; Strang et al., 2008

Acute or Acute on Chronic Pain

Work Group Recommendation: The first opioid prescription for acute pain should be no more than 20 low-dose, short-acting opioids or three days of medication, whichever is less. The total dose for acute pain should not exceed 100 morphine milligram equivalents (MME). For patients presenting in acute pain, already on chronic opioids, opioid tolerant or on methadone, use the same pill and dose limits as for opioid-naïve patients.

- **Benefit:** This limited dosing would reduce surplus opioid prescriptions as well as reduce potential of opioid abuse, overdose and diversion. It encourages frequent follow-up for pain requiring opioids and facilitates early recognition of aberrant opioid use.
- **Harm:** This limited dosing has potential to undertreat pain. It may cause inconvenience to patients by making them return to clinic for ongoing opioids and places some burden on providers arranging for early follow-up. In addition, some pain generators typically require more than three days of opioids.
- **Benefit-Harms Assessment:** The medical community has typically overprescribed opioids for acute pain to ensure that no patient is ever undertreated, but at the risk of providing surplus opioids to the patient and the community, and specifically harming those with vulnerability to opioids. Lowering the total quantity of opioids prescribed will prevent much of this harm, but in exchange some patients with ongoing pain will receive insufficient opioids, forcing them to return for evaluation from their primary clinician. While this may be a short-term burden to the patient and system, it will, over time, lessen the burden to patients and clinicians by decreasing the harms of opioids. Those already taking opioids chronically have higher tolerance and thus may receive less analgesia from opioids. These patients are also at a higher risk, may have more comorbidity, may already be on opioid doses known to have adverse effects, and are likely to have an opioid patient-provider agreement. Thus, while treating the opioid-tolerant patient with equivalent doses will provide less analgesia, it will also mitigate harms.
- **Relevant Resources:** Dowell, Haegerich, & Chou, 2016

Avoid Opioid Use for Chronic Pain

Work Group Recommendation: Avoid using opioids to treat patients with chronic pain.

- **Benefit:** This will lower the total opioid use in the United States and the corresponding harms from opioids. Opioids have no proven efficacy for chronic pain but do have known harms. Preventing chronic exposure to opioids is easier and preferable to detoxing a patient chronically on opioids.
- **Harm:** A subset of patients with chronic pain may benefit from chronic opioids. Patients already on chronic opioids cannot be easily detoxed from opioids, and this recommendation should not be taken as advice to detox existing chronic pain patients on long-term opioids.
- **Benefit-Harms Assessment:** Pain that has no easily identifiable pain generator, and no cure, is a daunting problem in medicine and causes great suffering. These patients try many modalities of care and too often end up on chronic opioid therapy. There are no proven benefits of opioids for most patients with chronic pain, but there are proven harms. Until further knowledge emerges, it is prudent to avoid initiating opioids in these patients.
- **Relevant Resources:** Chou et al., 2015; Chaparro et al., 2014; Manchikanti et al., 2006

Ongoing Treatment of Pain with Opioids

If the use of continued opioids is unavoidable, the Work Group members urge providers to consider the following issues.

Manage Dose Limits

Work Group Recommendation: Every effort should be made to keep chronic opioid using patients under 100 MME/day. Prescribers should consider seeking pain medicine consultation if greater than 100 MME is reached.

- **Benefit:** Opioid doses greater than 100 MME/day are associated with overdose death; as the dose increases, so do the risk and the strength of the associations.
- **Harm:** Some patients will have undertreated pain. Patients already on higher dose of opioids may struggle to lower their dose to a safe range. It is impossible to predict who will or will not overdose. Some patients who would not have been harmed by opioids will have their

dose limited.

- Benefit-Harms Assessment: Given a fairly clear dose response association between MME and death, patients should be kept under 100 MME/day, even at the cost of potentially undertreating pain in some.
- Relevant Resources: Han et al., 2015; Turner & Liang, 2015; Franklin et al., 2012; Gomes et al., 2011; Dunn et al., 2010

Work Group Recommendation: Opioids should be avoided for patients with substance use disorder or concomitant benzodiazepines use. If a patient with substance use disorder is prescribed opioids, the opioid dose should be less than 50 MME/day. If patient requires both opioids and benzodiazepines, opioids should be less than 50 MME/day, taking into careful consideration the benzodiazepine dose. There should be good communication among providers regarding dosing.

- Benefit: Patients with substance use disorder or benzodiazepine use are at higher risk of overdose if given opioids. Therefore, it is prudent to avoid opioids in these populations. If opioids are prescribed, the work group recommends a dose less than 50 MME/day to minimize adverse events.
- Harm: Some patients will have undertreated pain.
- Benefit-Harms Assessment: The risk of prescribing opioids to these populations outweighs the beneficial pain relief opioids may provide. Alternative pain management strategies should be employed.
- Relevant Resources: Han et al., 2015; Turner & Liang, 2015

Opioid Rotation and Conversion

Work Group Recommendation: Opioid conversion tables should be used only as guidance when changing opioids. Doses of the new opioid should be reduced by 50% of the previous daily MME dose and titrated to achieve analgesia.

- Benefit: This avoids overestimating opioid needs with a new opioid due to incomplete cross-tolerance and reduces the risk of adverse events and harm with the new opioid.
- Harm: Patients may not experience adequate pain relief if taking opioids chronically and may experience mild withdrawal until the new opioid can be titrated to effective dose. This dose reduction may lead to more frequent dose changes and clinic visits until adequate pain control is achieved.
- Benefit-Harms Assessment: Opioid conversion tables were developed from opioid-naïve patients and do not account for incomplete cross-tolerance in opioid-tolerant patients. Despite the chance of mild withdrawal, it is safer to underestimate the dose titrating as necessary than overestimate the dose causing harm.
- Relevant Resources: Pasternak, 2014; Vissers et al., 2010; Fine & Portenoy, 2009; Pasternak, 2005

Opioid Hyperalgesia

Methadone

Work Group Recommendation: Initiating an opioid-tolerant patient on methadone for chronic pain should be reserved for experienced clinicians who are familiar with its use because its long half-life is associated with overdose and death.

- Benefit: Trained clinicians are more familiar with the pharmacokinetic/pharmacodynamics properties of methadone and are better equipped to dose appropriately and provide the necessary monitoring to avoid adverse events.
- Harm: Clinicians trained in methadone prescribing may not be available to all patients who may benefit from methadone.
- Benefit-Harms Assessment: Methadone has a long and variable half-life that is not consistent between patients. It is highly lipophilic, and the respiratory depressant effect lasts longer than the analgesic effect. Methadone requires close follow-up and should only be initiated by clinicians experienced with its use.
- Relevant Resources: Wong & Walker, 2013; Chou et al., "Clinical guidelines," 2009

Fentanyl

Work Group Recommendation: Initiating transdermal fentanyl should be done only for patients with chronic opioid use greater than 60 MME daily, adequate subcutaneous adipose tissue and the cognitive ability to apply, remove and dispose of the patches safely. Patches should be removed after 72 hours, folded upon themselves sticky side inward and promptly flushed down the toilet. Sublingual fentanyl should be reserved for only those in need of palliative care for extreme pain and unable to take any alternatives.

- Benefit: Fentanyl patches are long-acting, renal-safe synthetic opioids, and as such they occupy a fairly unique niche in the opioid pharmacopeia. There are not many replacement medications.
- Harm: Fentanyl products are associated with accidental overdose deaths, including when an improperly disposed patch sticks to a toddler

or household pet. Transdermal fentanyl is unsafe in cachectic patients lacking adipose tissue, given fentanyl's lipophilicity. Sublingual (SL) fentanyl is exceedingly potent and apt to cause overdose if overused.

- Benefit-Harms Assessment: Fentanyl is a highly potent, lipophilic synthetic opioid that can be used to good effect treating pain if opioids are indicated. However, due to its high potency, fentanyl has caused accidental overdoses, and the transdermal patches need special handling and disposal instructions. Only patients with established opioid tolerance should receive fentanyl. Fentanyl SL formulations can be very helpful but are best reserved for those in pain in the dying process.
- Relevant Resources: U.S. Food and Drug Administration, 2013; U.S. Food and Drug Administration, 2012

Monitoring Considerations for Opioid Use

Prescription Monitoring Program (PMP)

Work Group Recommendation: The PMP should be queried in the following situations:

- If opioids are prescribed in dental, emergency department and urgent care settings, and when doses are changed.
- In every instance where there are concerns of substance use disorder, overdose, diversion, indeterminate pain disorder or polypharmacy.
- For those patients with an established stable dose of opioids for a chronically painful condition and a history of compliance with the prescriber, PMP checks should be at least twice per year.

Consider querying the PMP when initiating opioid therapy.

- Benefit: Detect clinician shopping, polypharmacy, opioid exposure and tolerance, and estimate the likely home supply of opioids. The PMP may reveal other prescribers whom to contact before prescribing opioids. A PMP query can help verify the patient's story. A PMP query affects clinician decision-making and may lower overall opioids prescribed and overdoses.
- Harm: PMP queries take time and training. Each state has a different program, with different laws governing their use, and incomplete cross-talk between states. Not every source of opioids is captured in a state PMP.
- Benefit-Harms Assessment: To query the PMP is yet another time and energy burden on medical providers, but it provides invaluable knowledge about the patient's exposure to opioids and other controlled substances, as well as other prescribers. Clinicians should know the loopholes and omissions inherent to their state's PMP.
- Relevant Resources: Han et al., 2015; Rutkow et al., 2015; Johnson et al., 2014; Albert et al., 2011

Urine Drug Screening

Work Group Recommendation: Routine random urine drug screens (UDS) for all patients on chronic opioid therapy for pain should be done at least once per year. UDS should be done if there is concern of aberrant behavior based on a prescriber's assessments and clinical judgment.

- Benefit: UDS can identify other substances being used that were not disclosed by the patient. UDS can identify when the patient is not taking the prescribed substance.
- Harm: UDS are costly. UDS have many false positives and negatives and may be difficult to interpret. Patients may not be prepared to provide a UDS. Use of UDS has not been shown to improve outcomes. UDS does not, in itself, make a diagnosis of substance use disorder or diversion.
- Benefit-Harms Assessment: Despite many complicating factors and lack of evidence that it improves outcomes, it is still standard of care, and universally recommended, that opioid prescribers check UDS on all patients routinely, and in any patient when there is concern of diversion or unsanctioned substance use. The ideal frequency and type of urine drug screen is not known.
- Relevant Resources: Dowell, Haegerich, & Chou, 2016; Starrels et al., 2012; Reisfield, Goldberger, & Bertholf, 2009; Michna et al., 2007; Heit & Gourlay, 2004

Visit Frequency

Work Group Recommendation: When initiating an opioid prescription, patients should be monitored within a month to evaluate harms and benefits, and assess treatment goals. Patients on stable opioid doses should be seen every three months.

- Benefit: Developing a strong relationship is important for both opioid prescribing and pain treatment. There is an increasing number of recommendations and regulations that apply to opioid prescribing. These can be time consuming and overwhelming to the patient if attempted on a single visit. Therefore, repeated education is necessary.
- Harm: There is not certain evidence that frequency of visits improves outcomes. Increasing frequency of visits may be burdensome to patients. Some patients have maintained stability on opioids with less frequent visits and may expect to continue the current expectations.
- Benefit-Harms Assessment: While there is a lack of definitive evidence, and this will consume health care resources and potentially burden

patients, increasing the frequency of visits for those receiving opioids, in particular those early in treatment for their pain, allows for many critical tasks to take place between provider and patient including education, screening and relationship building.

- Relevant Resources: Dowell, Haegerich, & Chou, 2016

Referrals for High-Risk Patients

Work Group Recommendation: Opioid prescribers should have a referral source for psychiatric treatment, substance use disorder treatment, physical therapy and pain medicine available if needed.

- Benefit: It is important to provide patients with a multidisciplinary approach to the treatment of pain when necessary. Multidisciplinary care may improve pain outcomes and mitigate the harms caused by mental health and addiction, specifically lowering the risk of inadvertent overdose and death.
- Harm: Access to addiction and psychiatric resource in the community may be sparse.
- Benefit-Harms Assessment: Patients with mental health and/or addictive disorders receiving opioids are at high risk for harm, including death. To safely treat such patients, prescribers perform better and have better outcomes if they have access to referrals for assessment and treatment of these disorders.
- Relevant Resources: Gaither et al., 2016; Reuben et al., 2015

If Opioid Use Disorder Is Suspected, Consider Referral to Addiction Medicine Specialist

Opioid Use Disorder Assessment

Work Group Recommendation: Opioid prescribers should recognize the symptoms of opioid use disorder. Opioid prescribers should understand the treatment options for opioid use disorder and have a referral source available.

- Benefit: Patients with opioid use disorder (OUD) receiving opioids for pain are at high risk of aberrant behavior and overdose death. Making the diagnosis of OUD and offering the proper referral for treatment may be a lifesaving intervention. Buprenorphine and methadone, given by a certified and trained specialist in their use, confers mortality benefit for patients with OUD. Intramuscular naltrexone decreases illicit use of opioids.
- Harm: Physicians are largely untrained at recognizing, counseling and treating patients with OUD. Referral options for medication-assisted therapy are sparse in many communities.
- Benefit-Harms Assessment: Of all the patients receiving opioids for pain, those with OUD are at the greatest risk of harm. Yet knowledge of diagnosis and treatment of OUD is insufficient among opioid prescribers. It is critical that providers take the time to become versed with this important risk factor of harm from opioids.
- Relevant Resources: Cousins et al., 2016; Gaither et al., 2016; Fullerton et al., 2014; Thomas et al., 2014; Carrieri et al., 2006

Offer Discontinuation of Opioids or Taper at Intervals of Six Months

Tapering Opioids

Work Group Recommendation: Once the patient and clinician agree to taper opioids, it should be individualized to the patient's circumstances, and a referral source should be available. While tapering opioids, patients should be offered additional treatment options and frequent follow-up.

Opioid tapering should be discussed and offered at intervals of six months for all patients on chronic opioids.

- Benefit: Each patient has unique reactions to opioids and exposure to them, making uniform tapering protocols impractical. Patient involvement in their own taper may improve outcomes. Intensified care during an opioid taper may improve patient-doctor communication and identify complications early.
- Harm: No good trial demonstrates how to best taper patients receiving opioids.
- Benefit-Harms Assessment: Guidelines and protocols are encouraging less use of opioids and emphasizing the harms of opioids but no one can say with certainty how to best taper a patient already on opioids. A reasonable recommendation is that providers work closely with patients, monitoring for risks, and individualize an opioid taper.
- Relevant Resources: Accurso & Rastegar, 2016; Dowell, Haegerich, & Chou, 2016; Berna, Kulich, & Rathmell, 2015

Clinical Algorithm(s)

The following detailed and annotated clinical algorithms are provided in the original guideline document (see the "Guideline Availability" field):

- Pain Assessment

- Pain Treatment Plan
- Acute Opioid Treatment
- Consideration for Continuing Opioid Treatment

Scope

Disease/Condition(s)

Pain (acute, subacute, and chronic), including dental/orofacial pain

Other Disease/Condition(s) Addressed

- Depression/anxiety disorder
- Substance use disorder (SUD)

Guideline Category

Counseling

Diagnosis

Evaluation

Management

Risk Assessment

Screening

Treatment

Clinical Specialty

Dentistry

Emergency Medicine

Family Practice

Geriatrics

Internal Medicine

Neurology

Obstetrics and Gynecology

Pharmacology

Psychiatry

Psychology

Intended Users

Advanced Practice Nurses

Allied Health Personnel

Dentists

Health Care Providers

Health Plans

Hospitals

Managed Care Organizations

Nurses

Pharmacists

Physician Assistants

Physicians

Psychologists/Non-physician Behavioral Health Clinicians

Substance Use Disorders Treatment Providers

Guideline Objective(s)

To provide guidance for assessment, diagnosis and treatment of acute, subacute, and chronic pain in ambulatory settings

Target Population

Adults age 18 years and older with non-cancer pain

Note: This guideline will not cover patients with migraines, active cancer, and/or those receiving palliative or hospice care. In addition, management of visceral pain is out of the scope of this guideline. Although much of the literature is overlapping with low back pain, this is not a primary focus of this guideline.

Interventions and Practices Considered

Diagnosis/Evaluation/Screening/Risk Assessment

1. Assessment of quality of life, function and pain intensity using validated tools
2. Determination of the pain generator
3. Diagnosis and treatment of dental/orofacial pain (ibuprofen plus acetaminophen)
4. Assessment of physical and behavioral health comorbidities
5. Screening for substance use

Treatment/Management

1. Developing a pain treatment plan
2. Psychotherapy strategies (e.g., cognitive behavioral therapy or mindfulness-based stress reduction)
3. Physical rehabilitation modalities (exercise)
4. Pharmacologic treatment (non-opioid medications)
5. Opioid management
 - Risk assessment using opioid risk assessment tools
 - Consideration for special populations (e.g., pregnant and lactating women, women of childbearing age, geriatrics)
 - Prescriber responsibility with opioid prescription (patient education, shared decision-making, safe use and disposal, type of opioid prescription used, patient-provider agreements [PPAs], offering naloxone)
 - Treatment of acute or acute on chronic pain
 - Avoiding opioids for chronic pain
 - Ongoing treatment of pain with opioids

- Monitoring considerations for opioid use (prescription monitoring programs, urine drug screening, visit frequency, referrals for high-risk patients, managing overdose)
- Discontinuation/tapering of opioids

Major Outcomes Considered

- Reliability and validity of screening and risk assessment tools
- Pain severity/intensity
- Overall functioning
- Quality of life
- Prevalence of mood and anxiety disorders
- Appropriateness opioid use
- Adverse effects of opioids
- Death from overdose

Methodology

Methods Used to Collect/Select the Evidence

Searches of Electronic Databases

Description of Methods Used to Collect/Select the Evidence

Literature Search

This guideline is based on a systematic evidence review evaluating literature published on Pain: Assessment, Non-Opioid Treatment Approaches and Opioid Management. The literature search included systematic reviews, randomized control trials, meta-analyses, observational studies, and protocols and/or guidelines for pain and/or opioids. The search included literature from January 1, 2010, through February 8, 2016.

The databases searched include PubMed and Cochrane. The search was limited to only studies in the English language and using human subjects. Other exclusions included cancer pain, migraine pain, palliative and end-of-life. The search included assessment, treatment and management of specific types of pain, specific modalities and specific medication classes. General categories are assessment of, treatment of and management of pain.

In addition to the literature searches, work group members and Institute for Clinical Systems Improvement (ICSI) staff obtained articles through individual searches. Those reviewed by the work group were included in the guideline where appropriate.

See the table in the original guideline document for the literature search terms comprising pain types, treatment modalities, and drugs.

Number of Source Documents

A total of 975 articles were identified from initial two literature searches; 481 articles were included as references, 161 of which support formal recommendations.

See the "Study Selection Flowchart" companion document (see the Availability of Companion Documents" field) for the flow of studies through the selection process.

Methods Used to Assess the Quality and Strength of the Evidence

Expert Consensus

Rating Scheme for the Strength of the Evidence

Not applicable

Methods Used to Analyze the Evidence

Review of Published Meta-Analyses

Systematic Review with Evidence Tables

Description of the Methods Used to Analyze the Evidence

In recent years, the Institute for Clinical Systems Improvement (ICSI) has transitioned to using a modified GRADE (Grading of Recommendations Assessment, Development and Evaluation) methodology as a way to systematically review the evidence and develop recommendations. After gathering the evidence through literature searches, the work group found a paucity of systematic reviews and randomized controlled trials (RCTs), making the application of GRADE methodology challenging. As an evolving field, there is still much about pain treatment, particularly use of opioids, that remains unstudied or understudied. Given this, GRADE methodology could not be applied to this document. Instead, the work group used the best available evidence to reach consensus recommendations. For each recommendation, the relevant resources used to support that recommendation are noted.

Methods Used to Formulate the Recommendations

Expert Consensus

Description of Methods Used to Formulate the Recommendations

Document Development and Revision Process

The development process is based on a number of long-proven approaches and is continually being revised based on changing community standards. The Institute for Clinical Systems Improvement (ICSI) staff, in consultation with the work group and a medical librarian, conduct a literature search to identify systematic reviews, randomized clinical trials, meta-analysis, other guidelines, regulatory statements and other pertinent literature.

The work group uses this information to develop or revise clinical flows and algorithms, write recommendations, and identify gaps in the literature. The work group gives consideration to the importance of many issues as they develop the guideline. These considerations include the systems of care in our community and how resources vary, the balance between benefits and harms of interventions, patient and community values, the autonomy of clinicians and patients and more. All decisions made by the work group are done using a consensus process.

ICSI's medical group members and sponsors review each guideline as part of the revision process. They provide comment on the scientific content, recommendations and implementation strategies. This feedback is used by and responded to by the work group as part of their revision work. Final review and approval of the guideline is done by ICSI's Committee on Evidence-Based Practice. This committee is made up of practicing clinicians and nurses, drawn from ICSI member medical groups.

Implementation Recommendations and Measures

These are provided to assist medical groups and others to implement the recommendations in the guidelines. Where possible, implementation strategies are included that have been formally evaluated and tested. Measures are included that may be used for quality improvement as well as for outcome reporting. When available, regulatory or publicly reported measures are included.

Document Revision Cycle

Scientific documents are revised as indicated by changes in clinical practice and literature. ICSI staff monitors major peer-reviewed journals for any pertinent evidence that would affect a particular guideline and recommendation.

Rating Scheme for the Strength of the Recommendations

Not applicable

Cost Analysis

The guideline developers reviewed published cost analyses.

Method of Guideline Validation

External Peer Review

Internal Peer Review

Description of Method of Guideline Validation

The Institute for Clinical Systems Improvement (ICSI) seeks review from members and the public during the revision process.

Member Review

All ICSI documents are available for member review at two points in the ICSI revision process. The ICSI Response Report is sent to members at the beginning of a document revision. The goal of this report is to solicit feedback about the guideline, including but not limited to the algorithm, content, recommendations, and implementation. Members are also welcome to participate in the public comment period (see below).

The work group would like to thank the following organizations for participating in the Pain: Assessment, Non-Opioid Treatment Approaches and Opioid Management pre-revision review:

- HealthPartners Medical Group, Bloomington, MN
- Hudson Physicians, Hudson, WI
- Medica Health Plan, Minnetonka, MN
- North Memorial Health Care, Minneapolis, MN
- Stillwater Medical Group, Stillwater, MN

Public Comment

ICSI makes a draft of the guideline available to the public on the ICSI Web site. The public is invited to comment in an effort to get feedback prior to its finalization. All comments will be reviewed by the ICSI facilitator and work group members as needed. ICSI work group may or may not make changes to the guideline based on public comment responses.

The work group would like to thank all those who took time to thoughtfully and thoroughly review the draft and submitted comments for the Pain: Assessment, Non-Opioid Treatment Approaches and Opioid Management guideline.

Invited Reviews

For some guidelines, ICSI will invite experts in the community to comment on a guideline draft prior to finalization. This is done during the public comment period.

The work group would like to thank all those who took time to thoughtfully and thoroughly review the draft and submitted comments for the Pain: Assessment, Non-Opioid Treatment Approaches and Opioid Management guideline.

- Miles Belgrade, MD, Comprehensive Pain Center; Head and Neck Pain Clinic; VA Health Care System

ICSI Patient Advisory Council (PAC)

The ICSI Patient Advisory Council responds to any guideline review requests put forth by ICSI facilitators and work groups. The PAC members may be involved at the beginning, middle, and/or end of the revision process. Patient advisors who serve on the council consistently share their experiences and perspectives in either a comprehensive or partial review of a document.

The PAC members provided thoughtful suggestions on additional places where clinicians could improve patient and family communication during the draft revision process that the work group was able to incorporate in the final document. The guideline work group is also pleased to announce that the Pain: Assessment, Non-Opioid Treatment Approaches and Opioid Management guideline has received the PAC Seal of Approval.

Document Approval

This document was approved by the Committee for Evidence-Based Practice (CEBP).

The committee reviewed and approved this guideline based on the following criteria:

- The aim(s) of the document is clearly and specifically described.
- The need for and importance of the document is clearly stated.
- The work group included individuals from all relevant professional groups and had the needed expertise.
- Patient views and preferences were sought and included.
- The work group has responded to all feedback and criticisms reasonably.
- Potential conflicts of interest were disclosed and do not detract from the quality of the document.
- Systematic methods were used to search for the evidence to assure completeness and currency.
- Health benefits, side effects, risks and patient preferences have been considered in formulating recommendations.
- The link between the recommendation and supporting evidence is clear.
- Where the evidence has not been well established, recommendations based on community practice or expert opinion are clearly identified.
- Recommendations are specific and unambiguous.
- Different options for clinical management are clearly presented.
- Clinical highlights and recommendations are easily identifiable.
- Implementation recommendations identify key strategies for *health care systems* to support implementation of the document.
- The document is supported with practical and useful tools to ease *clinician* implementation.
- Where local resource availability may vary, alternative recommendations are clear.
- Suggested measures are clear and useful for quality/process improvement efforts.

Once the document has been approved, it is posted on the ICSI Web site and released to members for use.

Evidence Supporting the Recommendations

References Supporting the Recommendations

Accurso AJ, Rastegar DA. The effect of a payer-mandated decrease in buprenorphine dose on aberrant drug tests and treatment retention among patients with opioid dependence. *J Subst Abuse Treat*. 2016 Feb;61:74-9. [PubMed](#)

Albert S, Brason FW 2nd, Sanford CK, Dasgupta N, Graham J, Lovette B. Project Lazarus: community-based overdose prevention in rural North Carolina. *Pain Med*. 2011 Jun;12 Suppl 2:S77-85.

American Geriatrics Society 2015 Beers Criteria Update Expert Panel. American Geriatrics Society 2015 updated Beers Criteria for potentially inappropriate medication use in older adults. *J Am Geriatr Soc*. 2015 Nov;63(11):2227-46. [42 references] [PubMed](#)

Argoff CE, Kahan M, Sellers EM. Preventing and managing aberrant drug-related behavior in primary care: systematic review of outcomes evidence. *J Opioid Manag*. 2014 Mar-Apr;10(2):119-34. [PubMed](#)

Arnold RM, Han PK, Seltzer D. Opioid contracts in chronic nonmalignant pain management: objectives and uncertainties. *Am J Med*. 2006 Apr;119(4):292-6. [PubMed](#)

Asmundson GJ, Katz J. Understanding the co-occurrence of anxiety disorders and chronic pain: state-of-the-art. *Depress Anxiety*. 2009;26(10):888-901.

Atluri S, Akbik H, Sudarshan G. Prevention of opioid abuse in chronic non-cancer pain: an algorithmic, evidence based approach. *Pain Physician*. 2012 Jul;15(3) [PubMed](#)

Berna C, Kulich RJ, Rathmell JP. Tapering long-term opioid therapy in chronic noncancer pain: evidence and recommendations for everyday practice. *Mayo Clin Proc*. 2015 Jun 1;90(6):828-42. [PubMed](#)

Bohnert AS, Valenstein M, Bair MJ, Ganoczy D, McCarthy JF, Ilgen MA, Blow FC. Association between opioid prescribing patterns and opioid overdose-related deaths. *JAMA*. 2011 Apr 6;305(13):1315-21. [PubMed](#)

Broderick JE, Junghaenel DU, Schwartz JE. Written emotional expression produces health benefits in fibromyalgia patients. *Psychosom Med*. 2005 Mar-Apr;67(2):326-34. [PubMed](#)

Broussard CS, Rasmussen SA, Reefhuis J, Friedman JM, Jann MW, Riehle-Colarusso T, Honein MA, National Birth Defects Prevention Study. Maternal treatment with opioid analgesics and risk for birth defects. *Am J Obstet Gynecol*. 2011 Apr;204(4):314.e1-11. [PubMed](#)

Butler SF, Cassidy TA, Chilcoat H, Black RA, Landau C, Budman SH, Coplan PM. Abuse rates and routes of administration of reformulated extended-release oxycodone: initial findings from a sentinel surveillance sample of individuals assessed for substance abuse treatment. *J Pain*. 2013 Apr;14(4):351-8. [PubMed](#)

Carrieri MP, Amass L, Lucas GM, Vlahov D, Wodak A, Woody GE. Buprenorphine use: the international experience. *Clin Infect Dis*. 2006 Dec 15;43 Suppl 4:S197-215. [PubMed](#)

Cassidy TA, DasMahapatra P, Black RA, Wieman MS, Butler SF. Changes in prevalence of prescription opioid abuse after introduction of an abuse-deterrent opioid formulation. *Pain Med*. 2014 Mar;15(3):440-51.

Castro MM, Daltro C, Kraychete DC, Lopes J. The cognitive behavioral therapy causes an improvement in quality of life in patients with chronic musculoskeletal pain. *Arq Neuropsiquiatr*. 2012 Nov;70(11):864-8. [PubMed](#)

Centers for Disease Control and Prevention (CDC). Adult use of prescription opioid pain medications - Utah, 2008. *MMWR Morb Mortal Wkly Rep*. 2010 Feb 19;59(6):153-7. [PubMed](#)

Centers for Disease Control and Prevention (CDC). Community-based opioid overdose prevention programs providing naloxone - United States, 2010. *MMWR Morb Mortal Wkly Rep*. 2012 Feb 17;61(6):101-5. [PubMed](#)

Chaparro LE, Furlan AD, Deshpande A, Mailis-Gagnon A, Atlas S, Turk DC. Opioids compared with placebo or other treatments for chronic low back pain: an update of the Cochrane Review. *Spine*. 2014 Apr 1;39(7):556-63. [PubMed](#)

Chou R, Turner JA, Devine EB, Hansen RN, Sullivan SD, Blazina I, Dana T, Bougatsos C, Deyo RA. The effectiveness and risks of long-term opioid therapy for chronic pain: a systematic review for a national institutes of health pathways to prevention workshop. *Ann Intern Med*. 2015 Feb 17;162(4):276-86. [PubMed](#)

Chou R, Fanciullo GJ, Fine PG, Adler JA, Ballantyne JC, Davies P, Donovan MI, Fishbain DA, Foley KM, Fudin J, Gilson AM, Kelter A, Mauskop A, O'Connor PG, Passik SD, Pasternak GW, Portenoy RK, Rich BA, Roberts RG, Todd KH, Miaskowski C, American Pain Society-American Academy of Pain Medicine Opioids Guidelines Panel. Clinical guidelines for the use of chronic opioid therapy in chronic noncancer pain. *J Pain*. 2009 Feb;10(2):113-30. [PubMed](#)

Chou R, Fanciullo GJ, Fine PG, Miaskowski C, Passik SD, Portenoy RK. Opioids for chronic noncancer pain: prediction and identification of aberrant drug-related behaviors: a review of the evidence for an American Pain Society and American Academy of Pain Medicine clinical practice guideline. *J Pain*. 2009 Feb;10(2):131-46.

Chou R, Qaseem A, Snow V, Casey D, Cross JT Jr, Shekelle P, Owens DK, Clinical Efficacy Assessment Subcommittee of the American College of Physicians, American College of Physicians, American Pain Society Low Back Pain Guidelines Panel. Diagnosis and treatment of low back pain: a joint clinical practice guideline from the American College of Physicians and the American Pain Society. *Ann Intern Med*. 2007 Oct 2;147(7):478-91. [PubMed](#)

Chu LF, Clark DJ, Angst MS. Opioid tolerance and hyperalgesia in chronic pain patients after one month of oral morphine therapy: a preliminary prospective study. *J Pain*. 2006 Jan;7(1):43-8. [PubMed](#)

Cicero TJ, Ellis MS, Surratt HL, Kurtz SP. The changing face of heroin use in the United States: a retrospective analysis of the past 50 years. *JAMA Psychiatry*. 2014 Jul 01;71(7):821-6. [PubMed](#)

Coffin PO, Behar E, Rowe C, Santos GM, Coffa D, Bald M, Vittinghoff E. Nonrandomized intervention study of naloxone coprescription for primary care patients receiving long-term opioid therapy for pain. *Ann Intern Med*. 2016 Aug 16;165(4):245-52. [PubMed](#)

Coffin PO, Sullivan SD. Cost-effectiveness of distributing naloxone to heroin users for lay overdose reversal. *Ann Intern Med*. 2013 Jan 1;158(1):1-9. [PubMed](#)

Coplan PM, Kale H, Sandstrom L, Landau C, Chilcoat HD. Changes in oxycodone and heroin exposures in the National Poison Data System after introduction of extended-release oxycodone with abuse-deterrent characteristics. *Pharmacoepidemiol Drug Saf*. 2013 Dec;22(12):1274-82. [PubMed](#)

Cousins G, Boland F, Courtney B, Barry J, Lyons S, Fahey T. Risk of mortality on and off methadone substitution treatment in primary care: a national cohort study. *Addiction*. 2016 Jan;111(1):73-82. [PubMed](#)

Cramer H, Lauche R, Hohmann C, L  dtke R, Haller H, Michalsen A, Langhorst J, Dobos G. Randomized-controlled trial comparing yoga and home-based exercise for chronic neck pain. *Clin J Pain*. 2013 Mar;29(3):216-23. [PubMed](#)

Cuesta-Vargas AI, Garc  a-Romero JC, Arroyo-Morales M, Diego-Acosta AM, Daly DJ. Exercise, manual therapy, and education with or without high-intensity deep-water running for nonspecific chronic low back pain: a pragmatic randomized controlled trial. *Am J Phys Med Rehabil*. 2011 Jul;90(7) [PubMed](#)

Cuesta-Vargas AI, White M, Gonz  lez-S  nchez M, Kuisma R. The optimal frequency of aquatic physiotherapy for individuals with chronic musculoskeletal pain: a randomised controlled trial. *Disabil Rehabil*. 2015;37(4):311-8. [PubMed](#)

Desai RJ, Hernandez-Diaz S, Bateman BT, Huybrechts KF. Increase in prescription opioid use during pregnancy among Medicaid-enrolled women. *Obstet Gynecol*. 2014 May;123(5):997-1002. [PubMed](#)

Desai RJ, Huybrechts KF, Hernandez-Diaz S, Mogun H, Paterno E, Kaltenbach K, Kerzner LS, Bateman BT. Exposure to prescription opioid analgesics in utero and risk of neonatal abstinence syndrome: population based cohort study. *BMJ*. 2015 May 14;350:h2102. [PubMed](#)

Dhalla IA, Mamdani MM, Sivilotti ML, Kopp A, Qureshi O, Juurlink DN. Prescribing of opioid analgesics and related mortality before and after the introduction of long-acting oxycodone. *CMAJ*. 2009 Dec 08;181(12):891-6. [PubMed](#)

Dowell D, Haegerich TM, Chou R. CDC guideline for prescribing opioids for chronic pain - United States, 2016. *MMWR Recomm Rep*. 2016 Mar 18;65(1):1-49. [223 references] [PubMed](#)

Dufour N, Thamsborg G, Oefeldt A, Lundsgaard C, Stender S. Treatment of chronic low back pain: a randomized, clinical trial comparing group-based multidisciplinary biopsychosocial rehabilitation and intensive individual therapist-assisted back muscle strengthening exercises.

Spine (Phila Pa 1976). 2010 Mar;35(5):469-76. [PubMed](#)

Dundar U, Solak O, Yigit I, Evcik D, Kavuncu V. Clinical effectiveness of aquatic exercise to treat chronic low back pain: a randomized controlled trial. Spine (Phila Pa 1976). 2009 Jun 15;34(14):1436-40. [18 references]

Dunn KM, Saunders KW, Rutter CM, Banta-Green CJ, Merrill JO, Sullivan MD, Weisner CM, Silverberg MJ, Campbell CI, Psaty BM, Von Korff M. Opioid prescriptions for chronic pain and overdose: a cohort study. Ann Intern Med. 2010 Jan 19;152(2):85-92. [PubMed](#)

Falla D, Lindström R, Rechter L, Boudreau S, Petzke F. Effectiveness of an 8-week exercise programme on pain and specificity of neck muscle activity in patients with chronic neck pain: A randomized controlled study. Eur J Pain. 2013 Nov;17(10):1517-28. [PubMed](#)

Fine PG, Portenoy RK, Ad Hoc Expert Panel on Evidence Review and Guidelines for Opioid Rotation. Establishing "best practices" for opioid rotation: conclusions of an expert panel. J Pain Symptom Manage. 2009 Sep;38(3):418-25. [PubMed](#)

Franklin GM, Mai J, Turner J, Sullivan M, Wickizer T, Fulton-Kehoe D. Bending the prescription opioid dosing and mortality curves: impact of the Washington State opioid dosing guideline. Am J Ind Med. 2012 Apr;55(4):325-31. [PubMed](#)

Fullerton CA, Kim M, Thomas CP, Lyman DR, Montejano LB, Dougherty RH, Daniels AS, Ghose SS, DelphinRittmon ME. Medication-assisted treatment with methadone: Assessing the evidence. Psychiatr Serv. 2014 Feb 1;65(2):146-57. [PubMed](#)

Gaither JR, Goulet JL, Becker WC, Crystal S, Edelman EJ, Gordon K, Kerns RD, Rimland D, Skanderson M, Justice AC, Fiellin DA. The association between receipt of guideline-concordant long-term opioid therapy and all-cause mortality. J Gen Intern Med. 2016 May;31(5):492-501. [PubMed](#)

Gatchel RJ, Okifuji A. Evidence-based scientific data documenting the treatment and cost-effectiveness of comprehensive pain programs for chronic nonmalignant pain. J Pain. 2006 Nov;7(11):779-93. [PubMed](#)

Gillis ME, Lumley MA, Mosley-Williams A, Leisen JC, Roehrs T. The health effects of at-home written emotional disclosure in fibromyalgia: a randomized trial. Ann Behav Med. 2006 Oct;32(2):135-46. [PubMed](#)

Gomes T, Mamdani MM, Dhalla IA, Michael Paterson J, Juurlink DN. Opioid dose and drug-related mortality in patients with nonmalignant pain. Arch Intern Med. 2011 Apr 11;171(7):686-91. [PubMed](#)

Gray SL, Anderson ML, Dublin S, Hanlon JT, Hubbard R, Walker R, Yu O, Crane PK, Larson EB. Cumulative use of strong anticholinergics and incident dementia: a prospective cohort study. JAMA Intern Med. 2015 Mar;175(3):401-7. [PubMed](#)

Grossman P, Tiefenthaler-Gilmer U, Raysz A, Kesper U. Mindfulness training as an intervention for fibromyalgia: evidence of postintervention and 3-year follow-up benefits in well-being. Psychother Psychosom. 2007;76(4):226-33. [PubMed](#)

Hall J, Swinkels A, Briddon J, McCabe CS. Does aquatic exercise relieve pain in adults with neurologic or musculoskeletal disease? A systematic review and meta-analysis of randomized controlled trials. Arch Phys Med Rehabil. 2008 May;89(5):873-83. [PubMed](#)

Han B, Compton WM, Jones CM, Cai R. Nonmedical prescription opioid use and use disorders among adults aged 18 through 64 years in the United States, 2003-2013. JAMA. 2015 Oct 13;314(14):1468-78. [PubMed](#)

Havens JR, Leukefeld CG, DeVaugh-Geiss AM, Coplan P, Chilcoat HD. The impact of a reformulation of extended-release oxycodone designed to deter abuse in a sample of prescription opioid abusers. Drug and Alcohol Dependence. 2014 Jun 01;139:9-17. [PubMed](#)

Hayden JA, van Tulder MW, Malmivaara A, Koes BW. Exercise therapy for treatment of non-specific low back pain. Cochrane Database Syst Rev. 2005;(3):CD000335. [149 references] [PubMed](#)

Heit HA, Gourlay DL. Urine drug testing in pain medicine. J Pain Symptom Manage. 2004 Mar;27(3):260-7. [PubMed](#)

Hooten WM, Lamer TJ, Twyner C. Opioid-induced hyperalgesia in community-dwelling adults with chronic pain. Pain. 2015 Jun;156(6):1145-52. [PubMed](#)

Hooten WM, St Sauver JL, McGree ME, Jacobson DJ, Warner DO. Incidence and risk factors for progression from short-term to episodic or long-term opioid prescribing: a population-based study. Mayo Clin Proc. 2015 Jul;90(7):850-6. [PubMed](#)

Hooten WM. Chronic pain and mental health disorders: shared neural mechanisms, epidemiology, and treatment. Mayo Clin Proc. 2016 Jul;91(7):955-70. [PubMed](#)

Hurwitz EL, Carragee EJ, van der Velde G, Carroll LJ, Nordin M, Guzman J, Peloso PM, Holm LW, Côté P, Hogg-Johnson S, Cassidy JD, Haldeman S, Bone and Joint Decade 2000-2010 Task Force on Neck Pain and Its Associated Disorders. Treatment of neck pain: noninvasive interventions: results of the Bone and Joint Decade 2000-2010 Task Force on Neck Pain and Its Associated Disorders. Spine (Phila Pa 1976). 2008 Feb 15;33(4 Suppl):S123-52. [PubMed](#)

Hwang CS, Chang HY, Alexander GC. Impact of abuse-deterrent OxyContin on prescription opioid utilization. Pharmacoepidemiol Drug Saf. 2015 Feb;24(2):197-204. [PubMed](#)

International Association for the Study of Pain. Classification of chronic pain: descriptions of chronic pain syndromes and definitions of pain terms. Second Edition. Washington (DC): International Association for the Study of Pain; [updated 2014 Aug 06];

Janssens KA, Zijlema WL, Joustra ML, Rosmalen JG. Mood and anxiety disorders in chronic fatigue syndrome, fibromyalgia, and irritable bowel syndrome: results from the LifeLines Cohort Study. Psychosom Med. 2015 May;77(4):449-57. [PubMed](#)

Johnson H, Paulozzi L, Porucznik C, Mack K, Herter B, Hal Johnson Consulting and Division of Disease Control and Health Promotion, Florida Department of H. Decline in drug overdose deaths after state policy changes - Florida, 2010-2012. MMWR Morb Mortal Wkly Rep. 2014 Jul 04;63(26):569-74. [PubMed](#)

Jones CM. Heroin use and heroin use risk behaviors among nonmedical users of prescription opioid pain relievers - United States, 2002-2004 and 2008-2010. Drug Alcohol Depend. 2013 Sep 1;132(1):95-100. [PubMed](#)

Jones T, Lookatch S, Grant P, McIntyre J, Moore T. Further validation of an opioid risk assessment tool: The Brief Risk Interview. J Opioid Manag. 2014 Sep 1;10(5):353-64. [PubMed](#)

Jones T, Moore T, Levy JL, Daffron S, Browder JH, Allen L, Passik SD. A comparison of various risk screening methods in predicting discharge from opioid treatment. Clin J Pain. 2012 Feb;28(2):93-100. [PubMed](#)

Juurlink DN, Dhalla IA. Dependence and addiction during chronic opioid therapy. J Med Toxicol. 2012;8(4):393-9. [PubMed](#)

Kamper SJ, Apeldoorn AT, Chiarotto A, Smeets RJ, Ostelo RW, Guzman J, van Tulder MW. Multidisciplinary biopsychosocial rehabilitation for chronic low back pain. Cochrane Database Syst Rev. 2014 Sep 2;(9):CD000963. [PubMed](#)

Keller S, Barn CM, Dodd SL, Schein J, Mendoza TR, Cleeland CS. Validity of the brief pain inventory for use in documenting the outcomes of patients with noncancer pain. Clin J Pain. 2004 Sep-Oct;20(5):309-18. [PubMed](#)

Koumantakis GA, Watson PJ, Oldham JA. Trunk muscle stabilization training plus general exercise versus general exercise only: randomized controlled trial of patients with recurrent low back pain. *Phys Ther*. 2005 Mar;85(3):209-25. [PubMed](#)

Liebschutz JM, Saitz R, Weiss RD, Averbuch T, Schwartz S, Meltzer EC, Claggett-Borne E, Cabral H, Samet JH. Clinical factors associated with prescription drug use disorder in urban primary care patients with chronic pain. *J Pain*. 2010 Nov;11(11):1047-55. [59 references]

Liu X, Ye W, Watson P, Tepper P. Use of benzodiazepines, hypnotics, and anxiolytics in major depressive disorder: Association with chronic pain diseases. *J Nerv Ment Dis*. 2010 Aug;198(8):544-50. [51 references]

Maeda A, Bateman BT, Clancy CR, Creanga AA, Leffert LR. Opioid abuse and dependence during pregnancy: temporal trends and obstetrical outcomes. *Anesthesiology*. 2014 Dec;121(6):1158-65. [PubMed](#)

Makris UE, Abrams RC, Gurland B, Reid MC. Management of persistent pain in the older patient: a clinical review. *JAMA*. 2014 Aug 27;312(8):825-36. [PubMed](#)

Manchikanti L, Abdi S, Atluri S, Balog CC, Benyamin RM, Boswell MV, Brown KR, Bruel BM, Bryce DA, Burks PA, Burton AW, Calodney AK, Caraway DL, Cash KA, Christo PJ, Damron KS, Datta S, Deer TR, Diwan S, Eriator I, Falco FJ, Fellows B, Geffert S, Gharibo CG, Glaser SE, Grider JS, Hameed H, Hameed M, Hansen H, Harned ME, Hayek SM, Helm 2nd S, Hirsch JA, Janata JW, Kaye AD, Kaye AM, Kloth DS, Koyyalagunta D, Lee M, Malla Y, Manchikanti KN, McManus CD, Pampati V, Parr AT, Pasupuleti R, Patel VB, Sehgal N, Silverman SM, Singh V, Smith HS, Snook LT, Solanki DR, Tracy DH, Vallejo R, Wargo BW, American Society of Interventional Pain Physicians. American Society of Interventional Pain Physicians (ASIPP) guidelines for responsible opioid prescribing in chronic non-cancer pain: Part I--evidence assessment. *Pain Physician*. 2012 Jul;15(3) [PubMed](#)

Manchikanti L, Cash KA, Damron KS, Manchukonda R, Pampati V, McManus CD. Controlled substance abuse and illicit drug use in chronic pain patients: An evaluation of multiple variables. *Pain Physician*. 2006 Jul;9(3):215-25.

Martell BA, O'Connor PG, Kerns RD, Becker WC, Morales KH, Kosten TR, Fiellin DA. Systematic review: opioid treatment for chronic back pain: prevalence, efficacy, and association with addiction. *Ann Intern Med*. 2007 Jan 16;146(2):116-27. [PubMed](#)

Michna E, Jamison RN, Pham LD, Ross EL, Janfaza D, Nedeljkovic SS, Narang S, Palombi D, Wasan AD. Urine toxicology screening among chronic pain patients on opioid therapy: frequency and predictability of abnormal findings. *Clin J Pain*. 2007 Feb;23(2):173-9. [PubMed](#)

Moore PA, Hersh EV. Combining ibuprofen and acetaminophen for acute pain management after third-molar extractions: translating clinical research to dental practice. *J Am Dent Assoc*. 2013 Aug;144(8):898-908. [PubMed](#)

Moore TM, Jones T, Browder JH, Daffron S, Passik SD. A comparison of common screening methods for predicting aberrant drug-related behavior among patients receiving opioids for chronic pain management. *Pain Med*. 2009 Nov/Dec;10(8):1426-33. [PubMed](#)

National Highway Traffic Safety Administration. Morphine (and heroin). [internet]. Washington (DC): National Highway Traffic Safety Administration; [accessed 2016 Jun 01].

Noble M, Treadwell JR, Tregear SJ, Coates VH, Wiffen PJ, Akafofomo C, Schoelles KM. Long-term opioid management for chronic noncancer pain. In: *Cochrane Database of Systematic Reviews*, Issue 1 [database online]. John Wiley & Sons, Ltd.; 2010 [accessed 2010 Jan 25]. [Art. No.: CD006605].

Nuckols TK, Anderson L, Popescu I, Diamant AL, Doyle B, Di Capua P, Chou R. Opioid prescribing: a systematic review and critical appraisal of guidelines for chronic pain. [Review]. *Ann Intern Med*. 2014 Jan 7;160(1):38-47.

Pasternak GW. Molecular biology of opioid analgesia. *J Pain Symptom Manage*. 2005 May;29(5 Suppl):S2-9. [PubMed](#)

Pasternak GW. Opiate pharmacology and relief of pain. *J Clin Oncol*. 2014 Jun 01;32(16):1655-61. [PubMed](#)

Petrov ME, Sawyer P, Kennedy R, Bradley LA, Allman RM. Benzodiazepine (BZD) use in community-dwelling older adults: Longitudinal associations with mobility, functioning, and pain. *Arch Gerontol Geriatr*. 2014 Sep-Oct;59(2):331-7. [PubMed](#)

Rainville J, Jouve CA, Hartigan C, Martinez E, Hipona M. Comparison of short- and long-term outcomes for aggressive spine rehabilitation delivered two versus three times per week. *Spine J*. 2002 Nov-Dec;2(6):402-7. [PubMed](#)

Reisfield GM, Goldberger BA, Bertholf RL. 'False-positive' and 'false-negative' test results in clinical urine drug testing. *Bioanalysis*. 2009 Aug;1(5):937-52. [PubMed](#)

Reuben DB, Alvanzo AAH, Ashikaga T, Bogat GA, Callahan CM, Ruffing V, Steffens DC. National Institutes of Health Pathways to Prevention Workshop: The role of opioids in the treatment of chronic pain. *Ann Intern Med*. 2015 Feb 17;162(4):295-300. [PubMed](#)

Richards BL, Whittle SL, van der Heijde DM, Buchbinder R. The efficacy and safety of muscle relaxants in inflammatory arthritis: a Cochrane systematic review. *J Rheumatol Suppl*. 2012 Sep;90:34-9. [PubMed](#)

Rolita L, Spegman A, Tang X, Cronstein BN. Increasing narcotic analgesic prescriptions for osteoarthritis is associated with increased falls and fractures in the elderly. *J Am Geriatr Soc*. 2013 Mar;61(3):335-40. [PubMed](#)

Rubin R. Analysis reveals large increase in hospitalizations in recent years among older patients prescribed opioids. *JAMA*. 2014 Oct 22-29;312(16):1621-3. [PubMed](#)

Rutkow L, Chang HY, Daubresse M, Webster DW, Stuart EA, Alexander GC. Effect of Florida's Prescription Drug Monitoring Program and pill mill laws on opioid prescribing and use. *JAMA Intern Med*. 2015 Oct;175(10):1642-9. [PubMed](#)

Saunders KW, Dunn KM, Merrill JO, Sullivan M, Weisner C, Braden JB, Psaty BM, Von Korff M. Relationship of opioid use and dosage levels to fractures in older chronic pain patients. *J Gen Intern Med*. 2010 Apr;25(4):310-15. [PubMed](#)

Schisler RE, Groninger H, Rosielle DA. Counseling patients on side effects and driving when starting opioids #248. *J Palliat Med*. 2012 Apr;15(4):484-5. [PubMed](#)

Sehgal N, Manchikanti L, Smith HS. Prescription opioid abuse in chronic pain: a review of opioid abuse predictors and strategies to curb opioid abuse. *Pain Physician*. 2012 Jul;15(3 Suppl):ES67-92. [PubMed](#)

Sessler NE, Downing JM, Kale H, Chilcoat HD, Baumgartner TF, Coplan PM. Reductions in reported deaths following the introduction of extended-release oxycodone (OxyContin) with an abuse-deterrent formulation. *Pharmacoepidemiol Drug Saf*. 2014 Dec;23(12):1238-46. [PubMed](#)

Severtson SG, Bartelson BB, Davis JM, et al. 92 difference in rates of abuse following reformulation of extended release oxycodone using data from the RADARSÂ® system poison center program. *Ann Emerg Med*. 2012;60:S34-35.

Severtson SG, Bartelson BB, Davis JM, Muñoz A, Schneider MF, Chilcoat H, Coplan PM, Surratt H, Dart RC. Reduced abuse, therapeutic errors, and diversion following reformulation of extended-release oxycodone in 2010. *J Pain*. 2013 Oct;14(10):1122-30. [PubMed](#)

Smyth J, Helm R. Focused expressive writing as self-help for stress and trauma. *J Clin Psychol*. 2003 Feb;59(2):227-35. [PubMed](#)

Solomon DH, Rassen JA, Glynn RJ, Garneau K, Levin R, Lee J, Schneeweiss S. The comparative safety of opioids for nonmalignant pain in older adults. *Arch Intern Med.* 2010 Dec 13;170(22):1979-86. [PubMed](#)

Spector W, Shaffer T, Potter DE, Correa-de-Araujo R, Rhona Limcangco M. Risk factors associated with the occurrence of fractures in U.S. nursing homes: resident and facility characteristics and prescription medications. *J Am Geriatr Soc.* 2007 Mar;55(3):327-33. [PubMed](#)

Standaert CJ, Friedly J, Erwin MW, Lee MJ, Rehtine G, Henrikson NB, Norvell DC. Comparative effectiveness of exercise, acupuncture, and spinal manipulation for low back pain. *Spine (Phila Pa 1976).* 2011 Oct 1;36(21 Suppl):S120-30. [PubMed](#)

Starrels JL, Fox AD, Kunins HV, Cunningham CO. They don't know what they don't know: Internal medicine residents' knowledge and confidence in urine drug test interpretation for patients with chronic pain. *J Gen Intern Med.* 2012 Nov;27(11):1521-7. [PubMed](#)

Starrels JL, Becker WC, Alford DP, Kapoor A, Williams AR, Turner BJ. Systematic review: treatment agreements and urine drug testing to reduce opioid misuse in patients with chronic pain. *Ann Intern Med.* 2010 Jun 1;152(11):712-20. [69 references] [PubMed](#)

Strang J, Manning V, Mayet S, Best D, Titherington E, Santana L, Offor E, Semmler C. Overdose training and take-home naloxone for opiate users: prospective cohort study of impact on knowledge and attitudes and subsequent management of overdoses. *Addiction.* 2008 Oct;103(10):1648-57. [PubMed](#)

Thomas CP, Fullerton CA, Kim M, Montejano L, Lyman DR, Dougherty RH, Daniels AS, Ghose SS, DelphinRittmon ME. Medication-assisted treatment with buprenorphine: assessing the evidence. *Psychiatr Serv.* 2014 Feb 1;65(2):158-70. [PubMed](#)

Turner BJ, Liang Y. Drug overdose in a retrospective cohort with non-cancer pain treated with opioids, antidepressants, and/or sedative-hypnotics: interactions with mental health disorders. *J Gen Intern Med.* 2015 Aug;30(8):1081-96. [PubMed](#)

Turner JA, Mancil L, Aaron LA. Short- and long-term efficacy of brief cognitive-behavioral therapy for patients with chronic temporomandibular disorder pain: a randomized, controlled trial. *Pain.* 2006 Apr;121(3):181-94. [PubMed](#)

U.S. Food and Drug Administration. FDA reminds the public about the potential for life-threatening harm from accidental exposure to fentanyl transdermal systems ("patches"). Silver Spring (MD): U.S. Food and Drug Administration; 2012 Apr 18

U.S. Food and Drug Administration. Fentanyl patch can be deadly to children. Silver Spring (MD): U.S. Food and Drug Administration; 2013 Sep 23

van Tulder MW, Touray T, Furlan AD, Solway S, Bouter LM. Muscle relaxants for non-specific low back pain. *Cochrane Database Syst Rev.* 2003;(2):CD004252. [PubMed](#)

Vestergaard P, Rejnmark L, Mosekilde L. Fracture risk associated with the use of morphine and opiates. *J Intern Med.* 2006 Jul;260(1):76-87. [PubMed](#)

Vincent K, Maigne JY, Fischhoff C, Lanlo O, Dagenais S. Systematic review of manual therapies for nonspecific neck pain. *Joint Bone Spine.* 2013 Oct;80(5):508-15. [PubMed](#)

Visser KCP, Besse K, Hans G, Devulder J, Morlion B. Opioid rotation in the management of chronic pain: Where is the evidence?. *Pain Pract.* 2010 Mar-Apr;10(2):85-93. [PubMed](#)

Volkow ND, Thomas McLellan A. Opioid abuse in chronic pain-misconceptions and mitigation strategies. *N Engl J Med.* 2016 Mar 31;374(13):1253-63. [PubMed](#)

Wasan AD, Michna E, Edwards RR, Katz JN, Nedeljkovic SS, Dolman AJ, Janfaza D, Isaac Z, Jamison RN. Psychiatric comorbidity is associated prospectively with diminished opioid analgesia and increased opioid misuse in patients with chronic low back pain. *Anesthesiology*. 2015 Oct;123(4):861-72. [PubMed](#)

Whiteman VE, Salemi JL, Mogos MF, Cain MA, Aliyu MH, Salihu HM. Maternal opioid drug use during pregnancy and its impact on perinatal morbidity, mortality, and the costs of medical care in the United States. *J Pregnancy*. 2014;2014:906723. [PubMed](#)

Wong E, Walker KA. A review of common methods to convert morphine to methadone. *J Community Hosp Intern Med Perspect*. 2013 Jan 7;2(4) [PubMed](#)

Yazdy MM, Mitchell AA, Tinker SC, Parker SE, Werler MM. Periconceptional use of opioids and the risk of neural tube defects. *Obstet Gynecol*. 2013 Oct;122(4):838-44. [PubMed](#)

Yokell MA, Green TC, Bowman S, McKenzie M, Rich JD. Opioid overdose prevention and naloxone distribution in Rhode Island. *Med Health R I*. 2011 Aug;94(8):240-2. [PubMed](#)

Type of Evidence Supporting the Recommendations

The type of supporting evidence is identified for each recommendation (see the original guideline document).

Benefits/Harms of Implementing the Guideline Recommendations

Potential Benefits

- Accurate assessment and diagnosis and appropriate treatment of pain, including prescription of opioids for pain and care of patients who are prescribed opioids
- Improved physical functioning, reduced disability, and reduced psychological distress and depression

See the "Benefits" and "Benefits-Harms Assessment" sections in the "Major Recommendations" field for additional benefits of specific interventions.

Potential Harms

See the "Harm" and "Benefits-Harms Assessment" sections in the "Major Recommendations" field for analysis of harms of specific interventions.

See also Appendices B and C in the original guideline document for additional information on adverse effects of non-opioid and opioid medications, respectively.

Contraindications

Contraindications

- Opioids should be avoided for patients with substance use disorder or concomitant benzodiazepines use.
- Breastfeeding is best avoided in infants when the mother is using higher doses or chronic administration of opioids.

See Appendices B and C in the original guideline document for additional information on precautions/contraindications to non-opioid and opioid medications, respectively.

Qualifying Statements

Qualifying Statements

- The information contained in this Institute for Clinical Systems Improvement (ICSI) Health Care Guideline is intended primarily for health professionals and other expert audiences.
- This ICSI Health Care Guideline should not be construed as medical advice or medical opinion related to any specific facts or circumstances. Patients and families are urged to consult a health care professional regarding their own situation and any specific medical questions they may have. In addition, they should seek assistance from a health care professional in interpreting this ICSI Health Care Guideline and applying it in their individual case.
- This ICSI Health Care Guideline is designed to assist clinicians by providing an analytical framework for the evaluation and treatment of patients, and is not intended either to replace a clinician's judgment or to establish a protocol for all patients with a particular condition.

Implementation of the Guideline

Description of Implementation Strategy

Implementation Recommendations

Prior to implementation, it is important to consider current organizational infrastructure that address the following:

- System and process design
- Training and education
- Culture and the need to shift values, beliefs and behaviors of the organization

The following system changes were identified by the guideline work group as key strategies for health care systems to incorporate in support of the implementation of this guideline:

- Communicate a clear and consistent message that clarifies:
 - Pain is a normal part of life, all pain is legitimate, and the goals are to improve function, quality of life and comfort.
 - Opioid usage is the last resort, and the benefits must outweigh the risk for each patient.
- Chronic pain should be managed proactively like any other chronic condition:
 - Develop a process to allow the patient to see a dedicated care team that has interest or expertise in chronic pain.
 - Develop relationships in the community and appropriate referral sources to create an interdisciplinary pain management team.
 - Develop protocols/work flows that guide clinicians to ensure consistent management of pain.

Implementation Tools

Chart Documentation/Checklists/Forms

Clinical Algorithm

Quality Measures

Quick Reference Guides/Physician Guides

Resources

For information about availability, see the *Availability of Companion Documents* and *Patient Resources* fields below.

Institute of Medicine (IOM) National Healthcare Quality Report Categories

IOM Care Need

Getting Better

Living with Illness

IOM Domain

Effectiveness

Patient-centeredness

Safety

Identifying Information and Availability

Bibliographic Source(s)

Hooten M, Thorson D, Bianco J, Bonte B, Clavel Jr A, Hora J, Johnson C, Kirksson E, Noonan MP, Reznikoff C, Schweim K, Wainio J, Walker N. Pain: assessment, non-opioid treatment approaches and opioid management. Bloomington (MN): Institute for Clinical Systems Improvement (ICSI); 2016 Sep. 160 p. [473 references]

Adaptation

Not applicable: The guideline was not adapted from another source.

Date Released

2016 Sep

Guideline Developer(s)

Institute for Clinical Systems Improvement - Nonprofit Organization

Guideline Developer Comment

The Institute for Clinical Systems Improvement (ICSI) is comprised of approximately 50 medical group and hospital members representing 8,500 clinicians in Minnesota and surrounding areas, and is sponsored by three nonprofit health plans. For a list of sponsors and participating organizations, see the [ICSI Web site](#) .

Source(s) of Funding

- The Institute for Clinical Systems Improvement (ICSI) provided the funding for this guideline revision. ICSI is a not-for-profit, quality improvement organization based in Bloomington, Minnesota. ICSI's work is funded by the annual dues of the member medical groups and three sponsoring health plans in Minnesota. Individuals on the work group are not paid by ICSI, but are supported by their medical group for this work.
- ICSI facilitates and coordinates the guideline development and revision process. ICSI, member medical groups, and sponsoring health plans review and provide feedback, but do not have editorial control over the work group. All recommendations are based on the work group's independent evaluation of the evidence.

Guideline Committee

Committee on Evidence-Based Practice

Pair: Assessment, Non-opioid Treatment Approaches and Opioid Management Work Group

Composition of Group That Authored the Guideline

Work Group Members: Michael Hooten, MD (*Work Group Leader*) (Mayo Clinic) (Anesthesiology); David Thorson, MD (*Work Group Leader*) (Entira Family Clinics) (Sports Medicine); Justin Hora, PharmD (Allina Medical Clinic) (Pharmacy); Chris Johnson, MD (Emergency Physicians, PA) (Emergency Medicine); Joseph Bianco, MD, FAAFP (Essentia Health) (Family Medicine); Kelly Schweim, PharmD (Fairview Health Services) (Medical Therapy Management); Neal Walker, RPh (Fairview Range Regional Health Care) (Pharmacy); Alfred Clavel, Jr., MD (HealthPartners Medical Group and Regions Hospital) (Neurology); Mary Pat Noonan, PhD (HealthPartners Medical Group and Regions Hospital) (Clinical Psychology); Charles Reznikoff, MD (Hennepin County Medical Center) (Internist, Addiction); Brian Bonte, DO (Hutchinson Health) (Family Medicine); John Wainio, DDS (Minnesota Dental Association) (General Dentistry); Eric Kirksson, MD (Twin Cities Orthopedics East Metro) (Physical Medicine and Rehabilitation); Audrey Hansen, BSN, MA, PMP (Institute for Clinical Systems Improvement [ICSI] Staff) (Project Manager/Health Care Consultant); Jodie Dvorkin, MD, MPH (ICSI Staff) (Project Manager/Health Care Consultant); Senka Hadzik (ICSI Staff) (Clinical Systems Improvement Facilitator)

Financial Disclosures/Conflicts of Interest

The Institute for Clinical Systems Improvement (ICSI) has long had a policy of transparency in declaring potential conflicting and competing interests of all individuals who participate in the development, revision and approval of ICSI guidelines and protocols.

In 2010, the ICSI Conflict of Interest Review Committee was established by the Board of Directors to review all disclosures and make recommendations to the board when steps should be taken to mitigate potential conflicts of interest, including recommendations regarding removal of work group members. This committee has adopted the Institute of Medicine Conflict of Interest standards as outlined in the report *Clinical Practice Guidelines We Can Trust* (2011).

Where there are work group members with identified potential conflicts, these are disclosed and discussed at the initial work group meeting. These members are expected to recuse themselves from related discussions or authorship of related recommendations, as directed by the Conflict of Interest committee or requested by the work group.

The complete ICSI policy regarding Conflicts of Interest is available at the [ICSI Web site](#) .

Disclosure of Potential Conflicts of Interest

Joseph Bianco, MD, FAAFP (Work Group Member)

Chief—Primary Care Process Department, Essentia Health

National, Regional, Local Committee Affiliations: Member of Essentia Health and St. Lewis Hospital Opioid Prescribing Group

Guideline Related Activities: None

Research Grants: None

Other: None

Brian Bonte, DO (Work Group Member)

Staff Physician, Family Medicine, Hutchinson Health

National, Regional, Local Committee Affiliations: Member of Counsel of Disability in Minnesota

Guideline Related Activities: None

Research Grants: None

Other: None

Alfred Clavel, Jr., MD (Work Group Member)

Department Head – Pain Management, Neurology, HealthPartners Medical Group and Regions Hospital

National, Regional, Local Committee Affiliations: None

Guideline Related Activities: None

Research Grants: None

Other: Received compensation for preparing a course on Preventing Chronic Pain for the University of Minnesota

Michael Hooten, MD (Work Group Leader)

Anesthesiology, Mayo Clinic

National, Regional, Local Committee Affiliations: None

Guideline Related Activities: None

Research Grants: None

Other: Consulting contract to guide the clinical trial design for Chrono Therapeutics, a division of Mayo Clinic beginning April 21, 2016

Justin Hora, PharmD (Work Group Member)

Clinical Pharmacist, Allina Medical Clinic

National, Regional, Local Committee Affiliations: None

Guideline Related Activities: None

Research Grants: None

Other: None

Chris Johnson, MD (Work Group Member)

Staff Physician, Emergency Medicine – Emergency Physicians, PA br /> National, Regional, Local Committee Affiliations: Member Minnesota Department of Human Services – Opioid Prescribing Work Group; Member Physicians for Responsible Opioid Prescribing

Guideline Related Activities: None

Research Grants: None

Other: None

Eric Kirksson, MD (Work Group Member)

Physical Medicine and Rehabilitation Physician – Twin Cities Orthopedics East Metro

National, Regional, Local Committee Affiliations: None

Guideline Related Activities: None

Research Grants: None

Other: None

Mary Pat Noonan, PhD, ABPP (Work Group Member)

Clinical Psychologist – HealthPartners Specialty Center, HealthPartners Medical Group and Regions Hospital

National, Regional, Local Committee Affiliations: Member of MN Department of Health – Advisory Panel on Intractable Pain and Medical Cannabis Use.

Guideline Related Activities: None

Research Grants: None

Other: None

Charles Reznikoff, MD (Work Group Member)

Assistant Professor of Medicine/Attending Physician, Internist, Addiction – Hennepin County Medical Center

National, Regional, Local Committee Affiliations: Steve Rummel Hope Foundation: Medical Advisory Board and Board of Directors; American College of Physicians-Scientific Planning Committee; Member Minnesota Department of Human Services- Opioid Prescribing Work Group

Guideline Related Activities: None

Research Grants: None

Other: Honorarium from Minnesota Medical Association for Opioids REMS (Risk Evaluation and Mitigation Strategies), and from Mayo and the State of Minnesota for teaching engagements. Dr. Reznikoff states that he donates all honoraria to charity.

Kelly Schweim, PharmD (Work Group Member)

Medical Therapy Management Provider – Fairview Health Services

National, Regional, Local Committee Affiliations: None

Guideline Related Activities: None

Research Grants: None

Other: None

David Thorson, MD (Work Group Leader)

Medical Director – Risk, Sports Medicine – Entira Family Clinics

National, Regional, Local Committee Affiliations: On the Minnesota Medical Association Board of Trustees and is President of the Minnesota

Medical Association (2015-2016). Member Advisory Councils for State of Minnesota Prescription Monitoring Management Program; Member Advisory Council, State of Minnesota HealthCare Home; Member UCare Physician Advisory Board; Member Board of PreferredOne Physician Association

Guideline Related Activities: Served on a multidisciplinary group for a longitudinal care program for Low Back Pain for the International Union of Operating Engineers Local Union #49

Research Grants: None

Other: None

Guideline Status

This is the current release of the guideline.

This guideline updates previous versions: Thorson D, Biewen P, Bonte B, Epstein H, Haake B, Hansen C, Hooten M, Hora J, Johnson C, Keeling F, Kokayeff A, Krebs E, Myers C, Nelson B, Noonan MP, Reznikoff C, Thiel M, Trujillo A, Van Pelt S, Wainio J. Acute pain assessment and opioid prescribing protocol. Health care protocol. Bloomington (MN): Institute for Clinical Systems Improvement (ICSI); 2014 Jan. 44 p. [76 references]

Hooten WM, Timming R, Belgrade M, Gaul J, Goertz M, Haake B, Myers C, Noonan MP, Owens J, Saeger L, Schweim K, Shteyman G, Walker N. Assessment and management of chronic pain. Bloomington (MN): Institute for Clinical Systems Improvement (ICSI); 2013 Nov. 105 p. [168 references]

This guideline meets NGC's 2013 (revised) inclusion criteria.

Guideline Availability

Available for purchase from the [Institute for Clinical Systems Improvement \(ICSI\) Web site](#) . Also available to ICSI members for free at the [ICSI Web site](#) and to Minnesota health care organizations free by request at the [ICSI Web site](#) .

Availability of Companion Documents

The following companions are provided to those who access the guideline (see the "Guideline Availability" field):

- Pain: assessment, non-opioid treatment approaches and opioid management. Executive summary. Bloomington (MN): Institute for Clinical Systems Improvement; 2016 Sep. 1 p.
- Pain: assessment, non-opioid treatment approaches and opioid management. Evidence table. Bloomington (MN): Institute for Clinical Systems Improvement; 2016 Sep. 5 p.
- Pain: assessment, non-opioid treatment approaches and opioid management. Study selection flowchart. Bloomington (MN): Institute for Clinical Systems Improvement; 2016 Sep. 1 p.
- Scientific document overview. Bloomington (MN): Institute for Clinical Systems Improvement; 2016 Feb 22. 4 p.

Additionally, the following are available in the appendices of the original guideline document:

- Aims and measures (quality measures)
- ABCDPQRS mnemonic
- Non-opioid pharmacology
- Opioid pharmacology, MME conversion factors, opioid rotation
- ICSI shared decision-making model
- PEG: a three-item scale assessing pain intensity and interference

Patient Resources

None available

NGC Status

This NGC summary was completed by ECRI Institute on April 21, 2014. This summary was updated by ECRI Institute on September 18, 2015 following the U.S. Food and Drug Administration advisory on non-aspirin nonsteroidal anti-inflammatory drugs (NSAIDs). This summary was updated by ECRI Institute on June 2, 2016 following the U.S. Food and Drug Administration advisory on Opioid pain medicines. This summary was updated by ECRI Institute on October 21, 2016 following the U.S. Food and Drug Administration advisory on opioid pain and cough medicines combined with benzodiazepines. This summary was updated by ECRI Institute on February 21, 2017. The updated information was verified by the guideline developer on March 27, 2017.

Copyright Statement

This NGC summary (abstracted Institute for Clinical Systems Improvement [ICSI] Guideline) is based on the original guideline, which is subject to the guideline developer's copyright restrictions.

The abstracted ICSI Guidelines contained in this Web site may be downloaded by any individual or organization. If the abstracted ICSI Guidelines are downloaded by an individual, the individual may not distribute copies to third parties.

If the abstracted ICSI Guidelines are downloaded by an organization, copies may be distributed to the organization's employees but may not be distributed outside of the organization without the prior written consent of the Institute for Clinical Systems Improvement, Inc.

All other copyright rights in the abstracted ICSI Guidelines are reserved by the Institute for Clinical Systems Improvement, Inc. The Institute for Clinical Systems Improvement, Inc. assumes no liability for any adaptations or revisions or modifications made to the abstracts of the ICSI Guidelines.

Disclaimer

NGC Disclaimer

The National Guideline Clearinghouse^{â„¢} (NGC) does not develop, produce, approve, or endorse the guidelines represented on this site.

All guidelines summarized by NGC and hosted on our site are produced under the auspices of medical specialty societies, relevant professional associations, public or private organizations, other government agencies, health care organizations or plans, and similar entities.

Guidelines represented on the NGC Web site are submitted by guideline developers, and are screened solely to determine that they meet the [NGC Inclusion Criteria](#).

NGC, AHRQ, and its contractor ECRI Institute make no warranties concerning the content or clinical efficacy or effectiveness of the clinical practice guidelines and related materials represented on this site. Moreover, the views and opinions of developers or authors of guidelines represented on this site do not necessarily state or reflect those of NGC, AHRQ, or its contractor ECRI Institute, and inclusion or hosting of guidelines in NGC may not be used for advertising or commercial endorsement purposes.

Readers with questions regarding guideline content are directed to contact the guideline developer.